C1 ant

- 2. (Amended) A method for inducing the formation of, or the maintenance or functional performance of lung tissue, comprising contacting the lung tissue with an amount of an agent effective to induce the formation of new lung tissue, wherein the agent is selected from a hedgehog antagonist, a ptc agonist, and an fgf-10 antagonist.
- 3. (Reiterated) The method of claim 1, wherein the lung tissue is in culture, and the agent is provided as a cell culture additive.
- 4. (Reiterated) The method of claim 1, wherein the cell is treated in an animal and the agent is administered to the animal as a therapeutic composition.
- 5. (Amended) The method of claim 1, wherein the agent is a hedgehog antagonist.
- 6. (Amended) The method of claim 5, wherein the *hedgehog* antagonist is a polypeptide including a *hedgehog* polypeptide sequence of at least an extracellular portion of a *hedgehog* polypeptide that binds to a *patched* polypeptide and blocks *hedgehog* signaling.
- 7. (Amended) The method of claim 6, wherein the polypeptide includes at least 50 amino acid residues of an N-terminal half of the *hedgehog* polypeptide.
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- 8. (Amended) The method of claims 6, wherein the polypeptide includes at least 100 amino acids of an extracellular domain of the *hedgehog* polypeptide.
- 9. (Amended) The method of claim 6, wherein the polypeptide includes at least a portion of the *hedgehog* polypeptide corresponding to a 19 kd fragment of an extracellular domain of the *hedgehog* polypeptide.
- 10. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide is encoded by a nucleic acid of a vertebrate organism.
- 11. (Reiterated) The method of claim 6, wherein the polypeptide includes a *hedgehog* polypeptide sequence represented in the general formula of SEQ ID No: 21.

- 12. (Reiterated) The method of claim 6, wherein the polypeptide includes a *hedgehog* polypeptide sequence represented in the general formula of SEQ ID No: 22.
- 13. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide is encoded by a human *hedgehog* nucleic acid.
- 14. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 60 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15 SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 15. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide sequence is encodable by a nucleic acid sequence which hybridizes under stringent conditions, including a wash step of 2.0X SSC at 50 °C, to a sequence selected from SEQ ID No:1, SEQ ID No:2, SEQ ID No:3, SEQ ID No:4, SEQ ID No:5, SEQ ID No:6, SEQ ID No:7, SEQ ID No:8, SEQ ID No:9, and SEQ ID No:19.
- 16. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide sequence is an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 17. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide sequence is an amino acid sequence of a Sonic *hedgehog* polypeptide.

Please add the following new claims.

22. (New) The method of claim 1 or 2, wherein the *hedgehog* antagonist, *patched* agonist, or *fgf-10* antagonist is a small organic molecule.

- 23. (New) The method of claim 5, wherein the *hedgehog* antagonist is a small organic molecule.
- 24. (New) The method of claim 5, further comprising preparing a formulation including an identified *hedgehog* antagonist and a pharmaceutically acceptable excipient.
- 25. (New) The method of claim 5, wherein the *hedgehog* antagonist binds to *hedgehog* and blocks *hedgehog* signal transduction.
- 26. (New) The method of claim 5, wherein the binding of the *hedgehog* antagonist prevents the upregulation of *patched* and/or *gli* expression.
- 27. (New) The method of claim 5, wherein the *hedgehog* antagonist decreases *hedgehog* signal transduction by altering the localization, protein-protein binding and/or enzymatic activity of an intracellular protein involved in a *hedgehog* signal transduction pathway.
- 28. (New) The method of claim 5, wherein the *hedgehog* antagonist alters the level of expression of a *hedgehog* protein, a *patched* protein or a protein involved in a *hedgehog* signal transduction pathway.
- 29. (New) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 75 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 30. (New) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 85 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 31. (New) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 90 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10,

SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

Cut Cont 32. (New) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 95 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

The amended claims are restated below to reflect changes from the last filing.

- 1. (Amended) A method for modulating the [growth state]proliferation, differentiation, or survival of lung tissue, or cells derived therefrom, comprising [ectopically] contacting the tissue with an amount of an agent effective to alter the [rate of] proliferation, differentiation, or survival of the lung tissue, wherein the agent is selected from [the group consisting of] a hedgehog [therapeutic]antagonist, a ptc [therapeutic]agonist, and an fgf-10 [therapeutic]antagonist.
- 2. (Amended) A method for inducing the formation of, or the maintenance or functional performance of lung tissue, comprising contacting the lung tissue with an amount of an agent effective to induce the formation of new lung tissue, wherein the agent is selected from [the group consisting of] a hedgehog [therapeutic]antagonist, a ptc [therapeutic]agonist, and an fgf-10 [therapeutic]antagonist.
- 5. (Amended) The method of claim 1, wherein the agent is a *hedgehog* [therapeutic]antagonist.
- 6. (Amended) The method of claim 5, wherein the *hedgehog* [therapeutic]<u>antagonist</u> is a polypeptide including a *hedgehog* polypeptide sequence of at least [a bioactive]<u>an</u> extracellular

portion of a *hedgehog* [protein]polypeptide that binds to a *patched* polypeptide and blocks *hedgehog* signaling.

- 7. (Amended) The method of claim 6, wherein the polypeptide includes at least 50 amino acid residues of an N-terminal half of the *hedgehog* [protein]polypeptide.
- 8. (Amended) The method of claims 6, wherein the polypeptide includes at least 100 amino acids of an extracellular domain of the *hedgehog* [protein]polypeptide.
- 9. (Amended) The method of claim 6, wherein the polypeptide includes at least a portion of the *hedgehog* [protein]polypeptide corresponding to a 19kd fragment of an extracellular domain of the *hedgehog* [protein] polypeptide.
- 10. (Amended) The method of claim 6, wherein the *hedgehog* [protein]<u>polypeptide</u> is encoded by a [gene]<u>nucleic acid of a vertebrate organism</u>.
- 13. (Amended) The method of claim 6, wherein the *hedgehog* [protein]polypeptide is encoded by a human *hedgehog* [gene]nucleic acid.
- 14. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 60 percent identical to an amino acid sequence of a *hedgehog* protein selected from [the group consisting of SEQ ID No:9,] SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15[and] SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 15. (Amended) The method of claim 6, wherein the *hedgehog* polypeptide sequence is encodable by a [nucleotide]nucleic acid sequence which hybridizes under stringent conditions, including a wash step of 2.0X SSC at 50°C, to a sequence selected from [the group consisting of] SEQ ID No:1, SEQ ID No:2, SEQ ID No:3, SEQ ID No:4, SEQ ID No:5, SEQ ID No:6, SEQ ID No:7, [and] SEQ ID No:8, SEQ ID No:9, and SEQ ID No:19.